

EFSA's Stakeholder Forum
November 20, 2018 ◇

*REACH- and OpenFoodTox-loaded
LRI Cheminformatic system
AMBIT2 supporting read-across*

◇
Dr Bruno Hubesch, LRI Programme Consultant



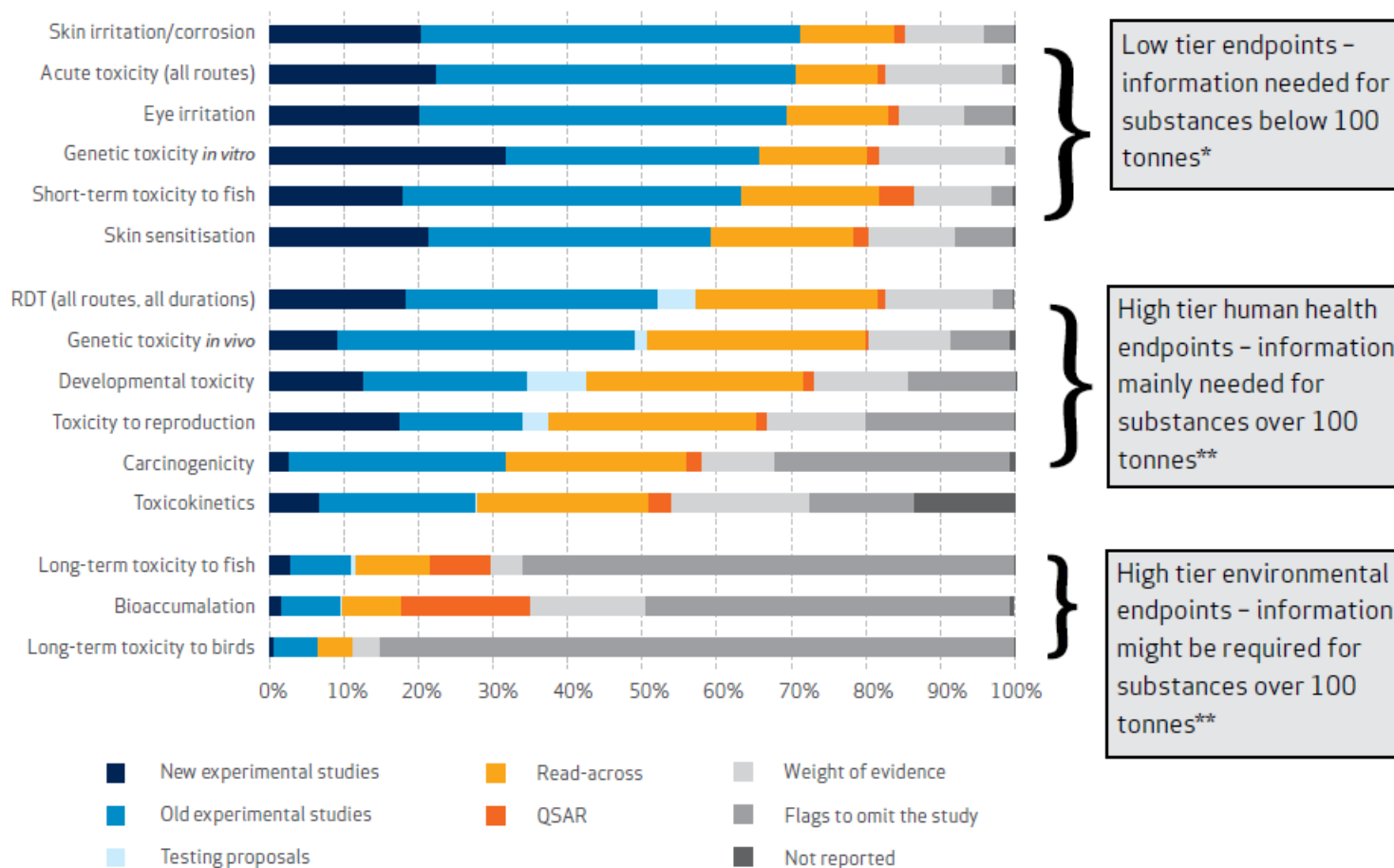
Cefic-LRI Programme 
European Chemical Industry Council - Cefic aisbl



Read-across and Category formation

- **Non-testing methods which are regularly applied to assess the safety of Chemicals**
 - Used on average in 20% of the Endpoint Study Records, while QSAR is used in < 1%
- **Accepted by most Regulatory Bodies if the approach taken is sufficiently justified and documented (RAAF-ECHA)**
- **Supported by in-silico tools** (see ECETOC, 2012, TR 116)
 - Using various methodologies like QSARs, rule-based predictions , similarity tools, etc.
- **Why LRI AMBIT** <https://ambitlri.ideaconsult.net/>
 - An in-silico tool developed continuously since 2005 (<http://ambit.sourceforge.net>)
 - Goal of the LRI EEM9.3-IC project was enhancing the predictive power of AMBIT
 - **Using large datasets of quality Substance data: ECHA & company DB & other sources**
 - Implementing workflows for Assessments supporting the assessor in setting up a read across/category approach and in establishing a valid justification for the approach
 - **Minimizing overall animal testing and resource costs by using available studies for other substances as well if appropriate**

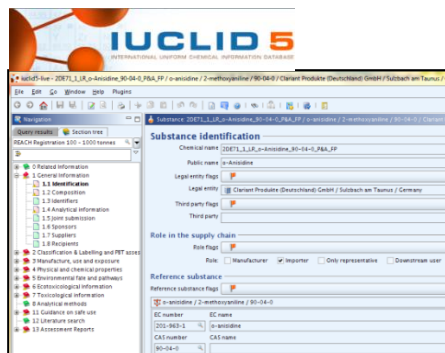
General aspects on non-testing approaches



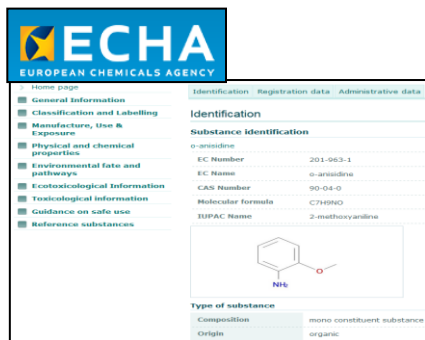
Options that registrants use to cover REACH information requirements for different data endpoints

Extract from "The use of alternatives to testing on animals for the REACH Regulation" Third Report under Article 117(3) of the REACH Regulation (2015)

LRI AMBIT2 Chemoinformatics System (Substances)



**Company IUCLID DB
& ECHA IUCLID DB
as
Major Data Sources**



ambit

**LRI AMBIT
Supporting
Read across &
Category formation**

**Transfer
of 14570
Dossiers**

*Data
transfer*

**Other Quality
Databases
(EFSA
Open Food Tox DB,...)**

*Data
transfer*



*Data
transfer*

**Other
Predictive
Tools**



Workflow for read across and category formation

5 MAIN STEPS

Assessment identifier	Collect structures	Endpoint data used	Assessment details	Report
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7 SUB STEPS

Assessment identifier	Collect structures	Endpoint data used	Assessment details	Report
	Collect structures	List of collected structures		

Assessment identifier	Collect structures	Endpoint data used	Assessment details	Report
		Search substance(s)	Selection of endpoints	

Assessment identifier	Collect structures	Endpoint data used	Assessment details		Report
			Initial matrix	Working matrix	Final matrix

Assessment identifier	Collect structures	Endpoint data used	Assessment details	Report
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AMBIT2: What's new?

- OpenFoodTox database from EFSA
- VEGA (courtesy E.Benfenati, Mario Negri Institute, Milano)
- NanoReg 1-2 database (i-Nano, 60 cpds)
- Open source, Application Programming Interface available
- Stand alone and web versions
- IUCLID6 compatible
- New and better functionalities
- And more...

AMBIT2 main functions

– *Search structures & Data*

- exact, similar, substructure
- combined with data search

– *Retrieval and management of IUCLID6 substance data*

- substance identification and composition
- Assigning structures to constituents, impurities ...
- 43 data endpoints of 14.570 substances

– *Read across/category formation*

- Workflows facilitates search for target and source structures, generating data matrices, gap filling and generating assessment reports with predefined formats automatically

– *Prediction tools / databases*

- VEGA models, Toxtree, Cramer rules, Protein binding / OpenFoodToxDB

– *Data management & exchange*

- flexible import/export of dataset
- manual upload of i6z files exported from IUCLID or semi-automatic import via IUCLID Web services.

Global marketing campaign /AMBIT2



1. **EU/Brussels**, April 20, 2017 (Article) Chemical Watch, “[Cefic’s AMBIT software tool reaching users around the globe”
2. **EU/Helsinki**, June 15-16, 2017: (Talk) ECOPA-SSCT Workshop 2017/CAAT-EU Academy, “Tools for Read-Across”
3. **US/ Seattle**, August 20-24, 2017: (Poster) WC10 / 10th World Congress on Alternatives & Animal Use
4. **Launch campaign**, Week Sept 4, 2017: LRI mailing list, website, Cefic Newsroom, Twitter, etc..
5. **EU/Bratislava**, September 11-14, 2017:(Poster) EUROTOX 2017
6. **EU/Brussels**, Sept 29, 2017: Hands-on Training Workshop at Cefic
7. **EU/Brussels**, Oct 5-6, 2017: (Talk) CAAT-EU Academy, “Use of *in silico* tools in chemical’s hazard assessment”
8. **EU/Milano**, October 19, 2017 : (Talk) LIFE COMBASE Workshop on *in silico* methods and biocides, Milan, PROSIL/LIFE project workshop (Mario Negri)
9. **EU/Helsinki**, Jan 18, 2018: ECHA staff training by Cefic LRI
10. **EU/Brussels**, Nov 20, 2018: EFSA Stakeholder Forum

Train yourself online!



Windows taskbar: File Explorer, Edge, Chrome, Firefox, etc. System tray: 9:32 AM, 13/06/2018, ENG.

Browser: http://cefic-lri.org/toolbox/ambit/

CEfic-LRI PROGRAMME | European Chemical Industry Council

CONTACT | WWW.CEFIC-ORG | MEMBERS PORTAL

LRI
Long-Range
Research Initiative

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AMBIT

AMBIT is an open chemoinformatic system designed to **support companies by facilitating chemical safety assessment**. Developed by Cefic-LRI, the software has the contribution of the European Chemicals Agency (ECHA) through sharing non-confidential REACH data to industry.

The AMBIT system consists of a **database including more than 450.000 chemical structures and REACH dataset of 14.570 substances**, which access was given to Cefic-LRI. AMBIT contributes to the safer use of chemicals and a reduction in testing and innovation cost by making it easier for companies to comply with regulations governing chemicals.

Users can search and access a wide range of existing information and prediction about a chemical. This process makes the tool both unique and powerful, particularly for data-poor small and medium sized enterprises (SMEs).

Several in-silico prediction models (e.g. Toxtree) are integrated in AMBIT. Molecular descriptors and structure alerts can be generated in the tool. The import and export function is enhanced in AMBIT, which allows communication with a variety of additional prediction models such as knowledge-based expert systems for toxicity and metabolism.

Publications

Mini guide to LRI funding

CEfic-LRI FUNDING

Events calendar

June 2018

SU	MO	TU	WE	TH	FR	SA
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23

AMBIT₃ ?

- **CompTox Dashboard** database from US EPA (700k chemicals)
- **TK integration** (IndusChemFate?, others), ADME's
- **FAME2** (Univ.Hamburg): predictive metabolism e-tool
- Open source, Application Programming Interface available
- Stand alone and web versions
- IUCLID n+1 New and better functionalities
- Platform/hub?
- 2019?
- And more...(REACH post 2018, METEOR, ToxRevDB-USEPA, PBT profiler, DIAMONDS, EPISUITE, ...)

AMBIT (1, 2,) 3: A READ-ACROSS FREE TOOL TO FACILITATE CHEMICAL SAFETY ASSESSMENT

- **Purpose:** make it easier for companies to comply with regulations governing chemicals
- Contains information on more than **450 000 chemical structures** from:
 - ECHA database (14 570 REACH dossiers)
 - EFSA OpenFoodTox database
 - **US EPA CompTox Dashboard**
- Accessed in **58 countries** around the world



Acknowledgements

- CEFIC LRI EEM9.3-IC
- Project idea for LRI EEM9.3-IC
 - **Volker Koch, Clariant (retired)**
 - **Joanna Jaworska, P&G (AMBIT 2005)**
- Project input :
 - **Clariant CompTox Team**
 - **Udo Jensch** (*Toxicologist*)
 - **Volker Koch** (*Ecotoxicologist*)
 - **Qiang Li** (*Toxicologist*)
 - **Joachim Schneider-Reigl** (*Ecotoxicologist*)
- Project implementation
 - **Ideaconsult Ltd.** www.ideaconsult.net
 - Nina Jeliaskova, Nikolay Kochev**

 **IDEAconsult Ltd.**



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Egon Willighagen



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THANK YOU!